

SEQUENCE LISTING

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NIO, NORIKI

<120> INHIBITORS OF ANGIOTENSIN CONVERTING ENZYME

<130> 239568US0CONT

<150> PCT/JP02/00194

<151> 2002-01-15

<150> JP 2001-7400

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<151> 2001-10-04

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<170> PatentIn version 3.1

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 Ser Ser Ala Leu Asp Met Ser Ile Ile Ser Tyr Asp Ser Ala His
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 gcg gac aag gcc gcc acg ttg cgc acc gag gag gag ctg atg tcc atg 138
 Ala Asp Lys Ala Ala Thr Leu Arg Thr Glu Glu Glu Leu Met Ser Met
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 tac gag cag tgg ctc gtg aag cac ggg aag gtg tac aac gcg ctc ggc 186
 Tyr Glu Gln Trp Leu Val Lys His Gly Lys Val Tyr Asn Ala Leu Gly

| | | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|-----|
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| gag | aag | gag | aag | cgc | ttc | cag | atc | ttc | aag | gac | aac | ctg | cga | ttc | atc | | 234 |
| Glu | Lys | Glu | Lys | Arg | Phe | Gln | Ile | Phe | Lys | Asp | Asn | Leu | Arg | Phe | Ile | | |
| -70 | | | | | -65 | | | | | -60 | | | | | -55 | | |
| gac | gac | cac | aac | tcc | gcg | gag | gac | cga | acc | tac | aag | ctc | gga | ctg | aac | | 282 |
| Asp | Asp | His | Asn | Ser | Ala | Glu | Asp | Arg | Thr | Tyr | Lys | Leu | Gly | Leu | Asn | | |
| | | | | -50 | | | | | -45 | | | | | -40 | | | |
| cgg | ttc | gct | gat | ctc | acc | aac | gag | gaa | tac | agg | gcc | aag | tac | ttg | gga | | 330 |
| Arg | Phe | Ala | Asp | Leu | Thr | Asn | Glu | Glu | Tyr | Arg | Ala | Lys | Tyr | Leu | Gly | | |
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| acc | aag | atc | gat | ccc | aac | cgg | agg | ctc | gga | aag | acc | ccg | agc | aac | cgc | | 378 |
| Thr | Lys | Ile | Asp | Pro | Asn | Arg | Arg | Leu | Gly | Lys | Thr | Pro | Ser | Asn | Arg | | |
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| tac | gcg | cca | cgt | gtc | ggc | gac | aaa | ttg | cct | gat | tcc | gtt | gat | tgg | agg | | 426 |
| Tyr | Ala | Pro | Arg | Val | Gly | Asp | Lys | Leu | Pro | Asp | Ser | Val | Asp | Trp | Arg | | |
| | -5 | | | | -1 | 1 | | | | 5 | | | | | 10 | | |
| aag | gaa | ggt | gct | gtt | cct | cct | gtc | aaa | gac | caa | gga | ggc | tgt | ggg | agc | | 474 |
| Lys | Glu | Gly | Ala | Val | Pro | Pro | Val | Lys | Asp | Gln | Gly | Gly | Cys | Gly | Ser | | |
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| tgt | tgg | gca | ttc | tca | gca | atc | ggt | gca | gta | gaa | gga | ata | aat | aag | ata | | 522 |
| Cys | Trp | Ala | Phe | Ser | Ala | Ile | Gly | Ala | Val | Glu | Gly | Ile | Asn | Lys | Ile | | |
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| gta | aca | ggc | gaa | ctg | att | tcg | tta | tca | gaa | caa | gaa | ttg | gtg | gat | tgt | | 570 |
| Val | Thr | Gly | Glu | Leu | Ile | Ser | Leu | Ser | Glu | Gln | Glu | Leu | Val | Asp | Cys | | |
| | | 45 | | | | | 50 | | | | | 55 | | | | | |
| gat | act | gga | tat | aac | caa | gga | tgc | aat | gga | gga | ctt | atg | gac | tat | gca | | 618 |
| Asp | Thr | Gly | Tyr | Asn | Gln | Gly | Cys | Asn | Gly | Gly | Leu | Met | Asp | Tyr | Ala | | |
| | 60 | | | | | 65 | | | | | 70 | | | | | | |
| ttt | gag | ttc | ata | atc | aac | aat | ggc | ggc | att | gat | tct | gat | gag | gat | tac | | 666 |
| Phe | Glu | Phe | Ile | Ile | Asn | Asn | Gly | Gly | Ile | Asp | Ser | Asp | Glu | Asp | Tyr | | |
| | | | | | 80 | | | | | 85 | | | | | 90 | | |
| cca | tac | cgt | ggt | gtt | gat | ggt | aga | tgc | gac | aca | tat | agg | aaa | aat | gct | | 714 |
| Pro | Tyr | Arg | Gly | Val | Asp | Gly | Arg | Cys | Asp | Thr | Tyr | Arg | Lys | Asn | Ala | | |
| | | | | 95 | | | | | 100 | | | | | 105 | | | |
| aaa | gtc | gtt | tct | att | gat | gac | tac | gaa | gat | gtt | cct | gcc | tat | gat | gag | | 762 |
| Lys | Val | Val | Ser | Ile | Asp | Asp | Tyr | Glu | Asp | Val | Pro | Ala | Tyr | Asp | Glu | | |
| | | | 110 | | | | | 115 | | | | | 120 | | | | |
| tta | gcc | ttg | aaa | aag | gcc | gtt | gca | aat | cag | ccc | gtg | agc | gtt | gct | att | | 810 |
| Leu | Ala | Leu | Lys | Lys | Ala | Val | Ala | Asn | Gln | Pro | Val | Ser | Val | Ala | Ile | | |

| 125 | | | | | 130 | | | | | 135 | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| gaa | gga | ggg | ggc | agg | gaa | ttt | caa | tta | tat | gta | tct | ggt | gta | ttc | acg | 858 |
| Glu | Gly | Gly | Gly | Arg | Glu | Phe | Gln | Leu | Tyr | Val | Ser | Gly | Val | Phe | Thr | |
| | 140 | | | | | 145 | | | | | 150 | | | | | |
| ggg | aga | tgt | ggc | aca | gca | cta | gat | cat | ggt | gtc | gtg | gct | gtt | ggg | tat | 906 |
| Gly | Arg | Cys | Gly | Thr | Ala | Leu | Asp | His | Gly | Val | Val | Ala | Val | Gly | Tyr | |
| | 155 | | | | 160 | | | | | 165 | | | | | 170 | |
| gga | aca | gct | aaa | ggt | cat | gat | tat | tgg | atc | gta | agg | aat | tca | tgg | ggt | 954 |
| Gly | Thr | Ala | Lys | Gly | His | Asp | Tyr | Trp | Ile | Val | Arg | Asn | Ser | Trp | Gly | |
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| tct | agc | tgg | gga | gag | gat | ggc | tac | atc | aga | tta | gaa | aga | aat | ctt | gct | 1002 |
| Ser | Ser | Trp | Gly | Glu | Asp | Gly | Tyr | Ile | Arg | Leu | Glu | Arg | Asn | Leu | Ala | |
| | | | 190 | | | | | 195 | | | | | 200 | | | |
| aac | agc | aga | tca | ggc | aag | tgt | gga | att | gca | att | gag | cca | tct | tat | ccc | 1050 |
| Asn | Ser | Arg | Ser | Gly | Lys | Cys | Gly | Ile | Ala | Ile | Glu | Pro | Ser | Tyr | Pro | |
| | | 205 | | | | | 210 | | | | | 215 | | | | |
| ctt | aag | aat | ggt | cca | aat | ccc | cct | aat | cct | gga | cca | tca | ccc | cct | tca | 1098 |
| Leu | Lys | Asn | Gly | Pro | Asn | Pro | Pro | Asn | Pro | Gly | Pro | Ser | Pro | Pro | Ser | |
| | 220 | | | | | 225 | | | | | 230 | | | | | |
| cct | gtg | aag | ccg | cca | aat | gtc | tgt | gac | aac | tac | tac | agc | tgt | gct | gat | 1146 |
| Pro | Val | Lys | Pro | Pro | Asn | Val | Cys | Asp | Asn | Tyr | Tyr | Ser | Cys | Ala | Asp | |
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| agt | gct | act | tgt | tgc | tgt | att | ttt | gag | ttc | gga | aat | gct | tgc | ttc | gag | 1194 |
| Ser | Ala | Thr | Cys | Cys | Cys | Ile | Phe | Glu | Phe | Gly | Asn | Ala | Cys | Phe | Glu | |
| | | | | 255 | | | | 260 | | | | | | 265 | | |
| tgg | ggt | tgc | tgt | cct | ctt | gag | ggt | gct | tcc | tgc | tgt | gat | gac | cac | tac | 1242 |
| Trp | Gly | Cys | Cys | Pro | Leu | Glu | Gly | Ala | Ser | Cys | Cys | Asp | Asp | His | Tyr | |
| | | | 270 | | | | | 275 | | | | | 280 | | | |
| agt | tgc | tgc | cct | gca | gac | tat | ccc | atc | tgc | aac | act | tac | gct | gga | act | 1290 |
| Ser | Cys | Cys | Pro | Ala | Asp | Tyr | Pro | Ile | Cys | Asn | Thr | Tyr | Ala | Gly | Thr | |
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| tgt | ctc | agg | agc | aag | aac | aac | ccc | ttt | gga | gtg | aag | gca | tta | agg | cgt | 1338 |
| Cys | Leu | Arg | Ser | Lys | Asn | Asn | Pro | Phe | Gly | Val | Lys | Ala | Leu | Arg | Arg | |
| | 300 | | | | | 305 | | | | | 310 | | | | | |
| act | cca | gcg | aaa | ccc | cat | tgg | acc | ttc | gga | cgt | aag | aac | aag | gtc | agc | 1386 |
| Thr | Pro | Ala | Lys | Pro | His | Trp | Thr | Phe | Gly | Arg | Lys | Asn | Lys | Val | Ser | |
| | 315 | | | | 320 | | | | | 325 | | | | | 330 | |
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Ala Asp Lys Ala Ala Thr Leu Arg Thr Glu Glu Glu Leu Met Ser Met
 -100 -95 -90

Tyr Glu Gln Trp Leu Val Lys His Gly Lys Val Tyr Asn Ala Leu Gly
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Glu Lys Glu Lys Arg Phe Gln Ile Phe Lys Asp Asn Leu Arg Phe Ile
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Asp Asp His Asn Ser Ala Glu Asp Arg Thr Tyr Lys Leu Gly Leu Asn
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Arg Phe Ala Asp Leu Thr Asn Glu Glu Tyr Arg Ala Lys Tyr Leu Gly
 -35 -30 -25

Thr Lys Ile Asp Pro Asn Arg Arg Leu Gly Lys Thr Pro Ser Asn Arg
 -20 -15 -10

Tyr Ala Pro Arg Val Gly Asp Lys Leu Pro Asp Ser Val Asp Trp Arg
 -5 -1 1 5 10

Lys Glu Gly Ala Val Pro Pro Val Lys Asp Gln Gly Gly Cys Gly Ser
 15 20 25

Cys Trp Ala Phe Ser Ala Ile Gly Ala Val Glu Gly Ile Asn Lys Ile
 30 35 40

| | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| Val | Thr | Gly | Glu | Leu | Ile | Ser | Leu | Ser | Glu | Gln | Glu | Leu | Val | Asp | Cys | |
| | | 45 | | | | | 50 | | | | | 55 | | | | |
| Asp | Thr | Gly | Tyr | Asn | Gln | Gly | Cys | Asn | Gly | Gly | Leu | Met | Asp | Tyr | Ala | |
| | 60 | | | | | 65 | | | | | 70 | | | | | |
| Phe | Glu | Phe | Ile | Ile | Asn | Asn | Gly | Gly | Ile | Asp | Ser | Asp | Glu | Asp | Tyr | |
| 75 | | | | | 80 | | | | | 85 | | | | | 90 | |
| Pro | Tyr | Arg | Gly | Val | Asp | Gly | Arg | Cys | Asp | Thr | Tyr | Arg | Lys | Asn | Ala | |
| | | | | 95 | | | | | 100 | | | | | 105 | | |
| Lys | Val | Val | Ser | Ile | Asp | Asp | Tyr | Glu | Asp | Val | Pro | Ala | Tyr | Asp | Glu | |
| | | | 110 | | | | | 115 | | | | | 120 | | | |
| Leu | Ala | Leu | Lys | Lys | Ala | Val | Ala | Asn | Gln | Pro | Val | Ser | Val | Ala | Ile | |
| | | 125 | | | | | 130 | | | | | 135 | | | | |
| Glu | Gly | Gly | Gly | Arg | Glu | Phe | Gln | Leu | Tyr | Val | Ser | Gly | Val | Phe | Thr | |
| | 140 | | | | | 145 | | | | | 150 | | | | | |
| Gly | Arg | Cys | Gly | Thr | Ala | Leu | Asp | His | Gly | Val | Val | Ala | Val | Gly | Tyr | |
| 155 | | | | | 160 | | | | | 165 | | | | | 170 | |
| Gly | Thr | Ala | Lys | Gly | His | Asp | Tyr | Trp | Ile | Val | Arg | Asn | Ser | Trp | Gly | |
| | | | | 175 | | | | | 180 | | | | | 185 | | |
| Ser | Ser | Trp | Gly | Glu | Asp | Gly | Tyr | Ile | Arg | Leu | Glu | Arg | Asn | Leu | Ala | |
| | | | 190 | | | | | 195 | | | | | 200 | | | |
| Asn | Ser | Arg | Ser | Gly | Lys | Cys | Gly | Ile | Ala | Ile | Glu | Pro | Ser | Tyr | Pro | |
| | | 205 | | | | | 210 | | | | | 215 | | | | |
| Leu | Lys | Asn | Gly | Pro | Asn | Pro | Pro | Asn | Pro | Gly | Pro | Ser | Pro | Pro | Ser | |
| | 220 | | | | | 225 | | | | | 230 | | | | | |
| Pro | Val | Lys | Pro | Pro | Asn | Val | Cys | Asp | Asn | Tyr | Tyr | Ser | Cys | Ala | Asp | |
| 235 | | | | | 240 | | | | | 245 | | | | | 250 | |

Ser Ala Thr Cys Cys Cys Ile Phe Glu Phe Gly Asn Ala Cys Phe Glu
 255 260 265

Trp Gly Cys Cys Pro Leu Glu Gly Ala Ser Cys Cys Asp Asp His Tyr
 270 275 280

Ser Cys Cys Pro Ala Asp Tyr Pro Ile Cys Asn Thr Tyr Ala Gly Thr
 285 290 295

Cys Leu Arg Ser Lys Asn Asn Pro Phe Gly Val Lys Ala Leu Arg Arg
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Thr Pro Ala Lys Pro His Trp Thr Phe Gly Arg Lys Asn Lys Val Ser
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Ser Ala

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 actcattagg caccaccaggc tttaactttt atgcttccgg atcgtatgtt gtgtggaatt 180
 gtgagcggat aacaatttca cacaggaaac agctatgacc atgattacgc caagcttgca 240
 tgccctgcagg tcgccctttc gtcttcaaga attcccctgt tgacaattaa tcatcgaact 300
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